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| 제 목 | Replication of Hepatitis B Virus is repressed by tumor suppressor p53 ( 과제; 간암 치료 신약 개발 및 이의 제제화 연구) |
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| 내 용 | |

Hepatitis B Virus (HBV) is a DNA virus with a 3.2kb partially double-stranded genome. The life cycle of the virus involves a reverse transcription of the greater than genome length 3.5kb mRNA. This pegenomic RNA contains all the genetic information encoded by the virus and functions as an intermediate in viral replication.

Tumor suppressor p53 has previously been shown to interact with the X-gene product of the HBV, which led us to hypothesize that p53 may act as a negative regulator of HBV replication and the role of the X-gene product is to overcome the p53-mediated restriction. As a first step to prove the above hypothesis, we tested whether p53 represses the propagation of HBV in *in vitro* replication system. By transient cotransfection of the plasmid containing a complete copy of the HBV genome and/or the plasmid encoding p53, we found that the replication of HBV is specifically blocked by wild-type p53. The levels of HBV DNA, HBs Ag and HBc/e Ag secreted in cell culture media were dramatically reduced upon coexpresion of wild-type p53 but not by the coexpression of the mutants of p53 (G154V and R273L). Furthermore, levels of RNAs originated from HBV genome were repressed more than 10 fold by the cotransfection of the p53 encoding plasmid. These results clearly states that p53 is a negative regulator of the HBV replication.

Next, to addresss the mechanism by which p53 represses the HBV replication, we performed the transient transfection experiments employing the pregenomic/core promotor-CAT(Chloramphenicol Acetyl Transferase) construct as a reporter. Cotransfection of wild-type p53 but not the mutant p53 expression plasmids repressed the CAT activity more than 8 fold. Integrating the above results, we propose that p53 represses the replication of HBV specifically by the down-regulation of the pregenomic/core promoter, which results in the reduced DNA synthesis of HBV. Currently, the mechanism by which HBV overcomes the observed p53-mediated restriction of replication is under investigation.